

## I. AMENDMENT

Please amend the claims as follows:

1. (Currently Amended) A method for depleting or isolating a targeted nucleic acid from a sample comprising:
  - a) incubating the sample with a first bridging oligonucleotide comprising (1) at least one bridging region comprising at least 5 nucleic acid residues and (2) at least one targeting region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the first targeting region and the targeted nucleic acid;
  - b) incubating the first bridging oligonucleotide with a capture oligonucleotide comprising a nonreacting structure and a capture region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the bridging region and the capture region; ~~and~~
  - c) isolating the targeted nucleic acid from the remainder of the sample; and,
  - d) discarding the targeted nucleic acid.
2. (Original) The method of claim 1 wherein the targeted nucleic acid is rRNA.
3. (Original) The method of claim 2, wherein the rRNA is prokaryotic 16S, prokaryotic 23S, eukaryotic 17S or 18S, or eukaryotic 28S rRNA.
4. (Original) The method of claim 3, wherein the rRNA comprises the sequence of SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62,

SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:71, SEQ ID NO:72, or SEQ ID NO:73.

5. (Original) The method of claim 1, wherein the sample comprises eukaryotic nucleic acid.
6. (Original) The method of claim 1, wherein the sample comprises prokaryotic nucleic acid.
7. (Original) The method of claim 6, wherein the prokaryotic nucleic acid is from a gram positive bacterium.
8. (Original) The method of claim 6, wherein the prokaryotic nucleic acid is from a gram negative bacterium.
9. (Original) The method of claim 1, wherein the bridging region, targeting region, or capture region comprises at least 10 nucleic acid residues.
10. (Original) The method of claim 9, wherein the bridging region, targeting region, or capture region comprises at least 15 nucleic acid residues.
11. (Original) The method of claim 10, wherein the bridging region, targeting region, or capture region comprises at least 20 nucleic acid residues.
12. (Original) The method of claim 1, wherein the bridging region or the capture region is polypurine or polypyrimidine.
13. (Original) The method of claim 12, wherein the bridging region is polypurine and the capture region is polypyrimidine.

14. (Original) The method of claim 1, further comprising incubating the sample with a second bridging oligonucleotide comprising (1) at least one bridging region comprising at least 5 nucleic acid residues and (2) at least one targeting region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the targeting region of the second bridging oligonucleotide and the targeted nucleic acid.

15. (Original) The method of claim 14, wherein the targeting region of the first bridging oligonucleotide is complementary to the sequence of a targeted nucleic acid and the targeting region of the second bridging oligonucleotide is complementary to a different sequence of a targeted nucleic acid.

16. (Original) The method of claim 15, wherein the targeting region of the first bridging oligonucleotide and the targeting region of the second bridging oligonucleotide are complementary to the same targeted nucleic acid.

17. (Original) The method of claim 15, wherein the targeting region of the first bridging oligonucleotide and the targeting region of the second bridging oligonucleotide are complementary to different targeted nucleic acids.

18. (Original) The method of claim 17, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of the largest rRNA molecule and the targeting region of the second bridging oligonucleotide is complementary to a sequence of the second largest rRNA molecule in the sample.

19. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 100 and 5000 residues of the 5' or 3' end of the targeted nucleic acid.

20. (Original) The method of claim 19, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 150 and 4000 residues of the 5' or 3' end of the targeted nucleic acid.

21. (Original) The method of claim 20, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 200 and 3000 residues of the 5' or 3' end of the targeted nucleic acid.
22. (Original) The method of claim 21, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 250 and 2000 residues of the 5' or 3' end of the targeted nucleic acid.
23. (Original) The method of claim 22, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 300 and 1500 residues of the 5' or 3' end of the targeted nucleic acid.
24. (Original) The method of claim 23, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 350 and 1000 residues of the 5' or 3' end of the targeted nucleic acid.
25. (Original) The method of claim 24, wherein targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 400 and 900 residues of the 5' or 3' end of the targeted nucleic acid.
26. (Original) The method of claim 25, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 450 and 800 residues of the 5' or 3' end of the targeted nucleic acid.
27. (Original) The method of claim 26, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence located between 500 and 700 residues of the 5' or 3' end of the targeted nucleic acid.
28. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence at the 3' or 5' end of the targeted nucleic acid.

29. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence not within 100 residues from the 3' or 5' end of the targeted nucleic acid.
30. (Original) The method of claim 14, wherein targeting region of the first or second bridging oligonucleotide hybridizes to a sequence not within 200 residues from the 3' or 5' end of the targeted nucleic acid.
31. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide hybridizes to a sequence not within 400 residues from the 3' or 5' ends of the targeted nucleic acid.
32. (Original) The method of claim 14, wherein the targeting region of the first or second bridging oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, or SEQ ID NO:22.
33. (Original) The method of claim 1, wherein the bridging oligonucleotide comprises a second targeting region comprising at least 5 nucleic acid residues complementary to a different sequence than the sequence to which the first targeting region is complementary.
34. (Original) The method of claim 33, wherein the first targeting region is complementary to a different targeting nucleic acid than the second targeting region is.
35. (Original) The method of claim 1, wherein the first bridging oligonucleotide comprises two bridging regions.

36. (Original) The method of claim 1, wherein the bridging oligonucleotide or the capture oligonucleotide is RNA, DNA, LNA, iso-bases, or a peptide nucleic acid.
37. (Original) The method of claim 1, further comprising washing the capture oligonucleotide after incubation with the sample and the bridging oligonucleotide.
38. (Original) The method of claim 1, wherein a) and b) are performed at the same temperature.
39. (Original) The method of claim 1, wherein a) and b) are performed at a different temperature.
40. (Original) The method of claim 38, wherein a) and b) are performed at the same time.
41. (Original) The method of claim 1, wherein the nonreacting structure comprises a bead comprising plastic, glass, teflon, silica, a magnet, cellulose, latex, polystyrene, nylon, cellulose, nitrocellulose, polymethacrylate, polyvinylchloride, or styrene-divinylbenzene
42. (Original) The method of claim 41, wherein isolating the targeted nucleic acid away from the sample comprises exposing the sample with the capture oligonucleotide to a magnetic field.
43. (Original) The method of claim 1, wherein the nonreacting structure is cellulose.
44. (Original) The method of claim 1, wherein the nonreacting structure is biotin.
45. (Original) The method of claim 44, wherein isolating the targeted nucleic acid comprises incubating the sample with streptavidin or avidin.

46. (Original) The method of claim 1, wherein the sample, capture oligonucleotide, and bridging oligonucleotide are incubated in a buffer comprising TMAC or TEAC.
47. (Cancelled)
48. (Currently Amended) The method of claim 2, further comprising:  
d) ~~discarding the targeted rRNA nucleic acid; and~~  
e) producing cDNA using mRNA in the remainder of the sample.
49. (Original) The method of claim 48, further comprising:  
f) attaching the cDNA to a solid support, wherein a nucleic acid array is created.
50. (Original) The method of claim 49, wherein the solid support is plastic, glass, or nylon.
51. (Original) The method of claim 50, wherein the solid support is a plate.
52. (Original) The method of claim 51, wherein the plate is a multiple-well plate.
53. (Original) The method of claim 48, further comprising:  
f) contacting a nucleic acid array with the cDNA.
54. (Currently Amended) A method for depleting rRNA from a sample comprising:  
a) incubating the sample with at least a first (1) bridging oligonucleotide comprising a bridging region comprising a poly-purine region of at least 5 residues and a targeting region comprising at least 5 contiguous nucleic acid residues complementary to a sequence of an rRNA molecule and a (2) capture oligonucleotide comprising a magnetic bead and a capture region comprising a poly-pyrimidine region of at least 5 residues, under conditions to allow hybridization between the bridging oligonucleotide and the capture oligonucleotide and the bridging oligonucleotide and the rRNA;

- b) incubating the sample with a magnetic bead; ~~and~~
- c) isolating the magnetic bead; and,
- d) discarding the magnetic bead with the rRNA.

55. (Withdrawn) A kit, in a suitable container means, comprising:

- a) a capture oligonucleotide comprising a capture region and a magnetic bead; and
- b) at least a first bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA.

56. (Withdrawn) The kit of claim 55, wherein the first bridging oligonucleotide comprises a second targeting region.

57. (Withdrawn) The kit of claim 56, wherein the first and second targeting regions have the same nucleic acid sequence.

58. (Withdrawn) The kit of claim 56, wherein the first and second targeting regions have different nucleic acid sequences.

59. (Withdrawn) The kit of claim 58, wherein the first targeting region is complementary to a sequence of an eukaryotic rRNA and the second targeting region is complementary to a sequence of a prokaryotic rRNA.

60. (Withdrawn) The kit of claim 58, wherein the first targeting region is complementary to a sequence of an eukaryotic rRNA and the second targeting region is complementary to a sequence of a different eukaryotic rRNA than the first targeting region.

61. (Withdrawn) The kit of claim 58, wherein the first targeting region is complementary to a sequence of a prokaryotic rRNA and the second targeting region is complementary to a sequence of a different prokaryotic rRNA than the first targeting region.



62. (Withdrawn) The kit of claim 55, further comprising a second bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA.

63. (Withdrawn) The kit of claim 62, wherein the targeting region of the second bridging oligonucleotide is complementary to a sequence of the same rRNA as the first targeting region.

64. (Withdrawn) The kit of claim 62, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of the largest rRNA and the targeting region of the second bridging oligonucleotide is complementary to a sequence of the second largest rRNA in the sample.

65. (Withdrawn) The kit of claim 62, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of an eukaryotic rRNA and the targeting region of the bridging oligonucleotide is complementary to a sequence of a prokaryotic rRNA.

66. (Withdrawn) The kit of claim 64, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of an eukaryotic 28S rRNA and the targeting region of the second bridging oligonucleotide is complementary to a sequence of a eukaryotic 17S or 18S rRNA.

67. (Withdrawn) The kit of claim 64, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of a prokaryotic 23S rRNA and the targeting region of the second bridging oligonucleotide is complementary to a sequence of a prokaryotic 16S rRNA.

68. (Withdrawn) The kit of claim 64, wherein the targeting region of the first bridging oligonucleotide is complementary to a sequence of an eukaryotic 28S rRNA and the targeting

region of the second bridging oligonucleotide is complementary to a sequence of a prokaryotic 23S rRNA.

69. (Withdrawn) The kit of claim 62, further comprising a third bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA.

70. (Withdrawn) The kit of claim 69, wherein the targeting region of the third bridging oligonucleotide is complementary to a sequence of a prokaryotic 23S rRNA.

71. (Withdrawn) The kit of claim 69, wherein the targeting region of the third bridging oligonucleotide is complementary to a sequence of a eukaryotic 18S rRNA.

72. (Withdrawn) The kit of claim 69, further comprising a fourth bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA.

73. (Withdrawn) The kit of claim 72, wherein (i) the targeting region of the first bridging oligonucleotide is complementary to a sequence of a prokaryotic 16S rRNA, (ii) the targeting region of the second bridging oligonucleotide is complementary to a sequence of a prokaryotic 23S rRNA, (iii) the targeting region of the third bridging oligonucleotide is complementary to a sequence of a eukaryotic 18S rRNA, and (iv) the targeting region of the fourth bridging oligonucleotide is complementary to a sequence of a eukaryotic 28S rRNA,

74. (Withdrawn) The kit of claim 55, wherein the first targeting region of the bridging oligonucleotide comprises SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, or SEQ ID NO:22.

75. (Withdrawn) The kit of claim 55, further comprising a buffer comprising TMAC or TEAC.
76. (Withdrawn) The kit of claim 55, further comprising a magnetic stand.
77. (Withdrawn) The kit of claim 55, further comprising:  
c) a solid support for preparing a nucleic acid array.
78. (Withdrawn) A bridging oligonucleotide comprising a (1) bridging region comprising a polypyrimidine or polypurine stretch and a (2) targeting region comprising at least 10 contiguous nucleic acid residues complementary to a sequence of an rRNA.
79. (Withdrawn) The oligonucleotide of claim 78, wherein the rRNA is eukaryotic.
80. (Withdrawn) The oligonucleotide of claim 79, wherein the rRNA is the 28S rRNA.
81. (Withdrawn) The oligonucleotide of claim 78, wherein the rRNA is prokaryotic.
82. (Withdrawn) The oligonucleotide of claim 81, wherein the rRNA is the 23S rRNA.
83. (Currently Amended) A method for depleting or isolating a targeted rRNA from a sample comprising:  
a) obtaining a the kit of claim 55; comprising: a capture oligonucleotide comprising a capture region and a magnetic bead; and at least a first bridging oligonucleotide comprising (1) at least one bridging region complementary to all or part of the capture region of the capture oligonucleotide and a (2) at least one targeting region comprising 10 contiguous nucleic acids complementary to a sequence of an rRNA;  
b) incubating the sample with the bridging oligonucleotide under conditions allowing hybridization between the targeting region and the targeted rRNA;

- c) incubating the bridging oligonucleotide with the capture oligonucleotide under conditions allowing hybridization between the bridging region and the capture region; and
- d) isolating the targeted rRNA from the remainder of the sample by incubating the sample with a magnetic field.

84. (Original) The method of claim 83, further comprising:

- e) obtaining the remainder of the sample enriched for mRNA;
- f) preparing cDNA from the mRNA.

85. (Original) The method of claim 84, further comprising:

- g) constructing a nucleic acid array with the cDNA.

## **II. RESPONSE TO OFFICE ACTION**

### **A. Status of the Claims**

Claims 1-54 and 83-85 were pending prior to the Office Action dated June 26, 2003. Claim 47 is cancelled, without prejudice or disclaimer. Claims 1, 48, and 83 have been amended. Support for the amendment of claim 1 may be found in originally filed claim 47. The amendment to claim 48 was made to address a redundancy in steps. The amendment to claim 83 incorporates the limitations of claim 55, from which claim 83 depended. Thus, no new matter has been added. Thus, claims 1-46, 48-54, and 83-85 are pending.

### **B. The Pending Claims Are Novel and Nonobvious over the Prior Art**

The Action rejected the pending claims as unpatentable over 35 U.S.C. § 102 and/or § 103 in view of a number of references. Applicants traverse these rejections and maintain that the originally filed claims are patentable over the cited references. They reserve the right to pursue such claims in a continuing application without acceding the nonpatentability of these claims.

In the Action it was indicated that claim 47 was allowable. Applicants have amended claim 1 essentially to incorporate the recitation of claim 47. Claim 47 depended from claim 1 and initially read:

- 47. The method of claim 1, further comprising:
  - d) discarding the portion of the sample that hybridizes to the capture oligonucleotide.

Applicants have amended claim 1 to add step d), such that claim 1 reads as follows:

- 1. A method for depleting or isolating a targeted nucleic acid from a sample comprising:
  - a) incubating the sample with a first bridging oligonucleotide comprising (1) at least one bridging region comprising at least 5 nucleic acid residues and (2) at least one targeting region comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the first targeting region and the targeted nucleic acid;
  - b) incubating the first bridging oligonucleotide with a capture oligonucleotide comprising a nonreacting structure and a capture region

- comprising at least 5 nucleic acid residues, under conditions allowing hybridization between the bridging region and the capture region; and
- c) isolating the targeted nucleic acid from the remainder of the sample; and,
- d) discarding the targeted nucleic acid.

Step d) from claim 47 was merely clarified in claim 1 to indicate that “the portion of the sample that hybridizes to the capture oligonucleotide” is the “targeted nucleic acid.”

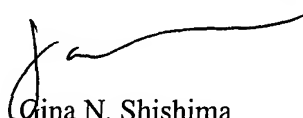
Accordingly, Applicants contend that claim 1 and all of its dependent claims are allowable over the cited art, as was indicated in the Action by the allowability of claim 47. Applicants respectfully request the art rejections be withdrawn.

### CONCLUSION

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants respectfully request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3081 is respectfully requested.

Respectfully submitted,



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